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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/786,015	04/09/2001	Peter Harrison	GJE-59	6391

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EXAMINER	
RAWLINGS, STEPHEN L	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 12/05/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/786,015	HARRISON, PETER	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *9 and 10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-10* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The amendment filed July 19, 2001 in Paper No. 7 is acknowledged and has been entered.

2. The election filed July 18, 2002 in Paper No. 11 is acknowledged and has been entered. Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 1-10 are pending in the application. Claims 9 and 10 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim.

4. Claims 1-8 are currently under prosecution.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for making a high-affinity anti-CEA sheep antibody, does not reasonably provide enablement for any high-affinity antibody. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claims are drawn to a high-affinity monoclonal antibody. More particularly the claims are drawn to a non-rodent high-affinity antibody, fragment, or derivative

thereof that binds to a tumor-associated antigen, specifically carcinoembryonic antigen (CEA).

The specification, however, only teaches a method for producing a monoclonal antibody and a recombinant derivative thereof that comprises immunizing sheep with CEA.

While the art has shown that sheep produce antibodies having very high affinities (see, for example, Groves, et al, *Hybridoma* **6**: 71-76, 1987), most other mammals and birds fail to produce antibodies that have binding affinity constants in the picomolar range. More typically monoclonal antibodies have binding affinity constants in the nanomolar range.

The exemplification of the production of antibodies by immunizing sheep with CEA is not reasonably commensurate in scope with the claims, as a substantial number of the claimed methods have not been exemplified in which rodent or other non-rodent high affinity antibodies are produced. Immunizing various animals with CEA or antigenic fragments thereof has produced many different antibodies having specific binding affinity for CEA, but generally the binding affinity of the antibodies produced by routine or conventional methodology is not expected to exceed 10^{-7} to 10^{-10} molar, expressed as the dissociation constant, but may vary depending upon the antigen and the animal immunized. The art teaches less routine or non-conventional methods for engineering recombinant antibodies having greater affinity for an antigen than a parent antibody from which the recombinant antibody is derived, but the specification provides an insufficient amount of guidance, direction, and exemplification to enable the skilled artisan to use such methodology to produce the claimed high affinity antibodies. Furthermore, because of the high unpredictability associated with the art, one could not immunize any animal other than sheep with any other antigen and reasonably expect to successfully produce antibodies having affinity equal to the affinity of the anti-CEA antibodies disclosed in the specification, because it is well known in the art that some antigens are not highly immunogenic, or display dominant epitopes to which low-affinity antibodies are produced. Therefore, even given the benefit of Applicant's disclosure one skilled in the art would not have a reasonable expectation of successfully producing

any high affinity antibody without having the need to perform additional, undue experimentation.

Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

7. Claims 2-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claim 2 is indefinite because the claims recites the limitation "wherein the amount of antibody bound in the second sample is > 60% of that bound in the first sample", but it is unclear after which step recited in claim 1 the limitation is required to be met. Accordingly, one of ordinary skill in the art would not be reasonably apprised of the metes and bound of the invention.

(b) Claim 5 is indefinite because the claim is not punctuated with a period.

(c) Claim 8 is indefinite because the claim recites the limitation "having at least the same properties determined by the steps in claim 1". Recitation of the limitation renders the claim indefinite because it is unclear to what subject matter the variant of the antibody is to be compared in determining whether both have at least the same properties. Accordingly, one of ordinary skill in the art would not be reasonably apprised of the metes and bound of the invention.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Groves, et al (*Hybridoma* **6**: 71-76, 1987).

Groves, et al teach an ovine monoclonal antibody that binds testosterone and has a very high affinity. The antibody of Groves, et al is deemed the same as the antibody of the instant claims, absent a showing of any differences.

Note: The Office does not have the facilities for examining and comparing Applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural, and functional characteristics as the claimed antibody. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed antibody is different than that taught by the prior art.

10. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Groves, et al (*Journal of Endocrinology* **126**: 217-222, 1990).

Groves, et al teach an ovine monoclonal antibody that binds progesterone and has a very high affinity. The antibody of Groves, et al is deemed the same as the antibody of the instant claims, absent a showing of any differences.

11. Claims 1-4, 7, and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Yang, et al (*Journal of Molecular Biology* **254**: 392-403, 1995).

Yang, et al teach a non-rodent Fab that binds the human envelope glycoprotein gp120 of HIV-1 and has a very high affinity. The antibody of Yang, et al is deemed the same as the claimed antibody or variant thereof, absent a showing of any differences.

12. Claims 1-5, 7 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Schier, et al (*Journal of Molecular Biology* **263**: 551-567, 1996).

Schier, et al teach a human single-chain Fv that binds the tumor-associated antigen ErbB2 and has a very high affinity. The antibody of Schier, et al is deemed the same as the claimed antibody or variant thereof, absent a showing of any differences.

13. Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Buchegger, et al (*Journal of the National Cancer Institute* **79**: 337-342, 1987).

Buchegger, et al teach an swine monoclonal antibody that binds CEA and has a very high affinity. The antibody of Buchegger, et al is deemed the same as the antibody of the instant claims, absent a showing of any differences.

14. Claims 1-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Osbourn, et al (*Immunotechnology* **2**: 181-196, 1996).

Osbourn, et al teach a human single-chain Fv that binds CEA and has a very high affinity. The antibody of Osbourn, et al is deemed the same as the antibody of the instant claims, absent a showing of any differences.

15. Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 91/01990 (Shively, et al).

Shively, et al teach a chimeric antibody that binds CEA and has a very high affinity. The antibody of Osbourn, et al is deemed the same as the antibody of the instant claims, absent a showing of any differences.

Double Patenting

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 1-8 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14, 19, and 22-24 of co-pending Application No. 09/786,013. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of claims 1-8 of the present application appears to be anticipated by the subject matter of claims 1-14, 19, and 22-24 of the co-pending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

18. No claims are allowed.

19. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Groves, et al (*Vet Immunol Immunopathol* **23**: 1-14, 1989) teaches means for producing non-rodent antibodies that are suitable for medicinal use. Adams, et al (*Cancer Res* **61**: 4750-4755, 2001) teaches limitations associated with the use of very high affinity antibodies.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (703) 305-3008. The examiner can normally be reached on Monday-Thursday, alternate Fridays, 8:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C. Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
November 26, 2002

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